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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,618	11/05/2003	MacDonald S. Morris	56297-5011-02	4873

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,618	MORRIS ET AL.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/4/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on September 4, 2007 has been entered. The claims pending in this application are claims 58-74. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the response filed on September 4, 2007.

Information Disclosure Statement

2. "Notice of Opposition" in the information disclosure statement filed on June 4, 2007 has been considered. Since this document has no publication date, it cannot be printed in the cover page of the patent if this instant case has been issued. Therefore, this document has been struck through in the 1449-form filed on June 4, 2007.

Claim Objections

3. Claim 58 is objected to because of the following informality: "non-target target tag nucleic acid" in (d) should be "non-target tag nucleic acid".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 58-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 58 is rejected as vague and indefinite. Since (d) of the claim does not require that the probes that have substantially uniform hybridization properties and do not cross-hybridize with non-target'target tag nucleic acids are from different oligonucleotide probe sets while preamble of the claim indicates that each oligonucleotide probe set comprises a plurality of individual nucleic acid probes all with the same nucleotide sequence, a plurality of individual nucleic acid probes in the same set must cross-hybridize each other. If the probes that have substantially uniform hybridization properties and do not cross-hybridize with non-target target tag nucleic acids in (d) of the claim is from the same set, the preamble and (d) of the claim do not correspond each other. Please clarify.

Response to Arguments

In page 5, last paragraph bridging to page 6, first paragraph of applicant's remarks, applicant argues that "the Examiner is of the opinion the preamble of the claim and step (d) are in conflict. Applicants respectfully disagree. The probes of the array have uniform hybridization properties both within a probe set, since those probes have the same target tag, and from probe set to probe set. For example, probes of a first probe set have uniform hybridization properties with probes of second, third, and fourth probe sets. Probes in the same probe set hybridize to the same target tag since they are of the same sequence, but they do not hybridize with the target tags corresponding to other probe sets (i.e. they do not cross-hybridize with **non-target** target

tags). The characteristics of the probes according to step (d) of the claim apply to all the probes of the array and not just to probes within a single probe set".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. Although applicant argues that "[T]he characteristics of the probes according to step (d) of the claim apply to all the probes of the array and not just to probes within a single probe set", since claim 58 does not indicate that the probes in (d) are from different oiligonucleotide probe sets, if the probes that have substantially uniform hybridization properties and do not cross-hybridize with non-target target tag nucleic acids in (d) of the claim are from the same set, the preamble and (d) of the claim do not correspond each other.

7. Claim 58 is rejected as vague and indefinite in view of the phrase "by the arrangement of at least two nucleotides" in (e) of the claim. Does this phrase means that each probe set on the array differs from every other probe set on the array by at least two nucleotides or mean something else? Please clarify.

Response to Arguments

In page 6, second paragraph of applicant's remarks, applicant argues that "[T]he Examiner would like clarification as to what is meant by the phrase. Applicants intend the phrase to require that each probe set of the array comprises a plurality of probes of the same sequence and that sequence differs from the probe sequence of the other probe sets on the array by at least two nucleotides".

These arguments have been fully considered but they are not persuasive toward the

withdrawal of the rejection because the phrase "by the arrangement of at least two nucleotides" in (e) of the claim is confusing. The examiner agrees to withdraw this rejection if applicant changes the phrase "by the arrangement of at least two nucleotides" to "by at least two nucleotides".

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 58-60, 63-66, and 68-73 are rejected under 35 U.S.C. 102(e) as being anticipated by Chee *et al.*, (US Patent No. 5,837,832, filed on March 16, 1995 with a priority date of June 25, 1993).

The applied reference has a common inventor, MacDonald S. Morris, with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Regarding claim 58, Chee *et al.*, teach a preselected array of oligonucleotides, the array comprising a spatially defined pattern of oligonucleotide probe sets (ie., at least four sets having

at least 100 probes and no more than 100,000 probes) on a solid support wherein each oligonucleotide probe set (ie., the first set) comprises a plurality of individual nucleic acid probes all with the same nucleotide sequence (see claim 1 in column 171), wherein the array contains more than 1000 different probes per cm^2 (ie., 2600 probes in 1.28 cm×1.28 cm area (1587 probes/cm^2), see column 18, third paragraph) as recited in (a). Since Chee *et al.,* teach that the at least four sets of probes contains at least one different nucleotide (see claim 1 in column 171) and the phrase "at least one different nucleotide" includes at least two different nucleotide, Chee *et al.,* disclose that each probe set on the array differs from every other probe set on the array by at least two nucleotides as recited in (e). Since it is known that melting temperature of an oligonucleotide is equal to 4 C°× (G+C) +2 C°×(A+T) (see attached Tm calculation for oligos), the difference in melting temperature of each set of probes (ie., having two nucleotide differences) on the array recited in the claim is 0 C° (ie., AT is replaced by TA or GC is replace by CG) or 2 C° (ie., GA is replaced by CG) or 4 C° (ie., AT is replaced by GC or GC is replaced by AT). Thus Chee *et al.,* disclose that the probes are selected to have a substantially similar melting temperature (ie., difference in 0 to 4 C°) as recited in (b). Since at least four sets on the array taught by Chee *et al.,* have at least 100 probes and no more than 100,000 probes (see claim 1 in column 117) which have ability to hybridize to a plurality of tag nucleic acids and the tag nucleic acids are not in the array and are not structural limitations of the array, Chee *et al.,* teach that each probe set hybridizes to one target tag nucleic acid under stringent hybridization conditions, the probes have substantially uniform hybridization properties and do not cross-hybridize with non-target target tag nucleic acids (ie., in certain hybridization conditions) and the

array contains probe sets complementary to at least 100 tag nucleic acids as recited in (c), (d), and (f).

Regarding claim 59, Chee *et al.,* teach that the probes are 20 nucleotide (see claim 1 in column 117). Since it is known that melting temperature of an oligonucleotide is equal to 4 C°× (G+C) +2 C°×(A+T) (see attached Tm calculation for oligos), the difference in melting temperature of each set of probes (ie., having two nucleotide differences) on the array recited in the claim is 0 C° (ie., AT is replaced by TA or GC is replace by CG) or 2 C° (ie., GA is replaced by CG) or 4 C° (ie., AT is replaced by GC or GC is replaced by AT). Thus Chee *et al.,* disclose that the melting temperatures of the probes are within plus (ie., +4 C° when AT is replaced by GC) or minus 7°C (ie., -4 C° when GC is replaced by AT).

Regarding claim 60, since Chee *et al.,* teach that the probes on the array have a length of 15 nucleotides and have 4-7 G+C when X is G (see claim 8 in columns 171 and 172) and the specification does not define "substantially identical", Chee *et al.,* disclose that the ratio of G+C bases in each probe (ie., the probes on the array having a length of 15 nucleotides and 4-7 G+C) is substantially identical.

Regarding claims 63-66, Chee *et al.,* teach that the probes are from about 8 to 150 nucleotides as recited in claim 63, the probes are between about 10 and 100 nucleotides as recited in claim 64, the probes are between about 15 and 30 nucleotides as recited in claim 65, and the probes are about 20 nucleotides as recited in claim 66 (see claim 1 in column 117).

Regarding claims 68-71, since at least four sets on the array taught by Chee *et al.,* have at least 100 probes and no more than 100,000 probes (see claim 1 in column 117) which have ability to hybridize to a plurality of tag nucleic acids and the tag nucleic acids are not in the array

and are not structural limitations of the array, Chee *et al.,* teach that the array contains probes complementary to between about 100 and about 100,000 tag nucleic acids as recited in claim 68, the array contains probes complementary to between about 5,000 and about 14,000 tag nucleic acids as recited in claim 69, the array contains probes complementary to between about 500 and about 15,000 tag nucleic acids as recited in claim 70, and the array contains probes complementary to between about 8,000 and about 9,000 tag nucleic acids as recited in claim 71.

Regarding claim 72, Chee *et al.,* teach that said array comprises a control probe (ie., one probe from three additional sets of probes, see claim 1 in column 117).

Regarding claim 73, Chee *et al.,* teach that said solid support is selected from the group consisting of slides, beads, polymeric chips, particles, strands, precipitates, gels, sheets, tubing, spheres, containers, capillaries, pads, slices, films and plates (ie., silica chip, see column 1, last paragraph).

Therefore, Chee *et al.,* teach all limitations recited in claims 58-60, 63-66, and 68-73.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 58, 60, 63, and 67-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drmanac (US Patent No. 6,401,267, priority date: September 8, 1994) in view of Davis *et al.,* (WO 90/11372, published on October 4, 1990).

Regarding claims 58, 60, and 74, Drmanac teach a preselected array of oligonucleotides, the array comprising a spatially defined pattern of oligonucleotide probe sets on a solid support (ie., a plurality of different oligonucleotides, see columns 8, 9, and 28) wherein each oligonucleotide probe set comprises a plurality of individual nucleic acid probes all with the same nucleotide sequence (ie., multiple copies of one of a plurality of different oligonucleotides with universal bases taught by Drmanac, see columns 8, 9, and 28) wherein the array contains more than 1000 different probes per cm^2 (ie.,$4^F/cm^2$, when F=7, $4^F/cm^2$=16,384 wherein F is length of the oligonucleotides, see column 3, lines 24-38 and column 11, lines 42-67) as recited in (a) of claim 58. Since a plurality of different oligonucleotides with universal bases on the array taught by Drmanac (see columns 8, 9, and 28) has an ability to hybridize with different nucleic acids, "stringent hybridization conditions" is relative term, and the claim do not require that tag nucleic acids are on the array, Drmanac discloses that each probe set hybridizes to one target tag nucleic acid under stringent hybridization conditions as recited in (c) of claim 58. Since an array comprising a plurality of different oligonucleotides with universal bases taught by Drmanac is used for sequencing by hybridization that requires specific hybridization (see columns 12 and 13), Drmanac discloses that the probes have substantially uniform hybridization properties and do not cross-hybridize with non-target target tag nucleic acids and the array contains probe sets complementary to at least 100 tag nucleic acids as recited in (d) and (f) of claim 58. Since a plurality of different oligonucleotides with universal bases taught by Drmanac comprise A, T, C, and G (see columns 8, 9, and 28) and the specification does not define "substantially identical", the ratio of G +C bases in each probe (ie., a plurality of different oligonucleotides with universal bases taught by Drmanac) is considered to be substantially

identical as recited in claim 60 so that the probes are selected to have a substantially similar melting temperature as recited in (b) of claim 58. Since Drmanac teaches a kit comprising a labeled probe that hybridizes to the array (see column 9, lines 1-20), Drmanac discloses a kit comprising the array comprising (a) to (d) and (f) of claim 58 as recited in claim 74.

Regarding claim 63, Drmanac teaches that the probes are from about 8 to 150 nucleotides (ie., 9 bp, see column 9, lines 7-20).

Regarding claim 67-71, Drmanac teaches that the array contains more than 10,000 probe sets per cm^2 as recited in claim 67 (ie.,$4^F/cm^2$, when F=7, $4^F/cm^2$=16,384 wherein F is length of the oligonucleotides, see column 3, lines 24-38 and column 11, lines 42-67). Since the array taught by Drmanac has and no more than 200,000 probes (ie., $4^F/cm^2$, when F=9, $4^F/cm^2$=262,144 wherein F is length of the oligonucleotides, see column 3, lines 24-38 and column 11, lines 42-67) which have ability to hybridize to a plurality of tag nucleic acids and the tag nucleic acids are not in the array and are not structural limitations of the array, Drmanac teaches that the array contains probes complementary to between about 100 and about 100,000 tag nucleic acids as recited in claim 68, the array contains probes complementary to between about 5,000 and about 14,000 tag nucleic acids as recited in claim 69, the array contains probes complementary to between about 500 and about 15,000 tag nucleic acids as recited in claim 70, and the array contains probes complementary to between about 8,000 and about 9,000 tag nucleic acids as recited in claim 71.

Regarding claim 72, Drmanac teaches that the array comprises control probes (i.e., one of a plurality of different probes taught by Drmanac).

Regarding claim 73, Drmanac teaches that said solid support is selected from the group consisting of slides, beads, polymeric chips, particles, strands, precipitates, gels, sheets, tubing, spheres, containers, capillaries, pads, slices, films and plates (ie., glass plate, see column 15, fifth paragraph).

Drmanac does not disclose that each probe set on the array differs from every other probe set on the array by the arrangement of at least two nucleotides as recited in (e) of claims 58 and 74.

Davis *et al.,* teach a plurality of different oligonucleotide probes with at least two nucleotide difference (see page 23, lines 19-27 to page 24, line 1 and claims 38-40 in pages 77 and 78).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made the array as recited in claim 58 and the kit recited in claim 74 wherein each probe set on the array differs from every other probe set on the array by the arrangement of at least two nucleotides in view of prior art of Drmanac and Davis *et al.*. One having ordinary skill in the art has been motivated to do so because optimization of numbers of variable nucleotides in plurality of different oligonucleotides on an array during the process for constructing the array recited in claim 58 and the kit recited in claim 74, in the absence of convincing evidence to the contrary, would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to construct an array as recited in claim 58 and the kit recited in claim 74 so that each probe set on the array differs from every other probe set on the array by the arrangement of at least two nucleotides.

More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).

12. Claims 64-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drmanac in view of Davis *et al.,* as applied to claims 58-60, 63-66, and 68-73 above, and further in view of Wallace (WO 93/25563, published on December 23, 1993).

The teachings of Drmanac and Davis *et al.,* have been summarized previously, *supra*.

Drmanac and Davis *et al.,* do not disclose that the probes are between about 10 and 100 nucleotides as recited in claim 64, the probes are between about 15 and 30 nucleotides as recited in claim 65, and the probes are about 20 nucleotides as recited in claim 66.

Wallace teaches an array (ie., the grid) having the probes are 20 nucleotides (see page 12, and 14-16).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made the array as recited in claims 64-66 wherein the probes are between about 10 and 100 nucleotides, the probes are between about 15 and 30 nucleotides and the probes are about 20 nucleotides in view of prior art of Drmanac, Davis *et al.,* and Wallace. One having ordinary skill in the art has been motivated to do so because optimization of the length of a plurality of different oligonucleotides on an array during the process for constructing the array recited in claims 64-66, in the absence of convincing evidence

to the contrary, would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to construct the array as recited in claims 64-66. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).

Conclusion

13. No claim is allowed.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

November 8, 2007

FRANK LU
PRIMARY EXAMINER